Cultivating liver cells on printed arrays of hepatocyte growth factor.

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Public Summary:

Scientific Abstract:
Growth factors are commonly present in soluble form during in vitro cell cultivation experiments in order to provide signals for cellular proliferation or differentiation. In contrast to these traditional experiments, we investigated solid-phase presentation of a hepatocyte growth factor (HGF), a protein important in liver development and regeneration, on microarrays of extracellular matrix (ECM) proteins. In our experiments, HGF was mixed in solution with ECM proteins (collagen (I), (IV) or laminin) and robotically printed onto silane-modified glass slides. Primary rat hepatocytes were seeded onto HGF/ECM protein microarrays and formed cellular clusters that corresponded in size to the dimensions of individual protein spots (500 microm diameter). Analysis of liver-specific products, albumin and alpha1-antitrypsin, revealed several fold higher levels of expression of these proteins in hepatocytes cultured on HGF/ECM microarrays compared to cells cultivated on ECM proteins alone. In addition, cultivation of hepatocytes on HGF/ECM protein spots led to spontaneous reorganization of cellular clusters from a monolayer into three-dimensional spheroids. We also investigated the effects of surface-tethered HGF on hepatocytes co-cultivated with stromal cells and observed a significantly higher level of albumin in co-cultures where hepatocytes were stimulated by HGF/ECM spots compared to co-cultures created on ECM protein islands without the growth factor. In summary, our study suggests that incorporation of HGF into ECM protein microarrays has a profound and long-lasting effect on the morphology and phenotype of primary hepatocytes. In the future, the number of growth factors printed on ECM microarrays will be expanded to enable multiplexed and combinatorial screening of inducers of cellular differentiation or proliferation.